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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,340	12/04/2003	Dirk Jager	LUD-5793.1 CIP	3224

24972 7590 09/29/2006

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EXAMINER	
HALVORSON, MARK	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 09/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/729,340	JAGER ET AL.	
	Examiner	Art Unit	
	Mark Halvorson	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10-14,58-60,83-92,113 and 114* is/are pending in the application.

4a) Of the above claim(s) *1,10-12,14,83,84,87-91 and 113* is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,58-60,85 and 86* is/are rejected.

7)☒ Claim(s) *92 and 114* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *sequence search*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II in the reply filed on August 21, 2006 is acknowledged. Applicant's election of the peptide of SEQ ID NO:32 encoded by the nucleic acid of SEQ ID NO:31 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1, 10-12, 14, 83, 84, 87-91 and 113 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claims 13, 58-60, 85, 86, 92 and 114 are under prosecution.

Specification

3. The disclosure is objected to because of the following informalities: The Related Applications section of the specification has not been updated. The updated status for applications 60/430,869, 10/181,663, 09/602,362 and 09/451,739 have not been provided. Appropriate correction is required.

Claim Objections

4. Claims 114 is objected to for being dependent on a non-elected claim. For purposes of this action, the limitations of claim 113 are included in claim 114 to the

extent that they are drawn to the elected invention. However, this treatment does not relieve Applicant the burden of responding to this objection.

5. Claim 92 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 58-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the claim language in Claims 58-60 are vague as it is not clear what is encompassed by the claimed composition. For example, the composition of Claim 58 comprises "at least one peptide consisting of an amino acid sequence of from 8 to 25 amino acids concatenated to each other in the isolated cancer associated cancer antigen of claim 13". So, at the very least, it would appear that the immunogenic composition comprises at least one peptide that is 8 amino acids long. But, what is the nexus between this peptide and the cancer antigen of Claim 13? It's not clear if these peptides are obtained from or are fragments of SEQ ID NO:13 or if they are in some

type of mixture. Hence, the metes and bounds of the claims cannot be adequately determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 58-60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the peptides LLSHGAVIEV, SLSKILDTV, and SLDQKLFQL, does not reasonably provide enablement for any 8 to 25 amino acid peptide of SEQ ID NO:32. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a composition comprising at least one peptide consisting of an amino acid sequence of from 8 to 25 amino acids concatenated to each other in the isolated cancer associated antigen and a pharmaceutically acceptable adjuvant.

The specification discloses that three peptides bind to HLA-A2 molecules and stimulate CD8 T cells to secrete lymphokines in vitro (paragraphs 82, 83, 92 and 93).

The specification contemplates the peptides to bind to MHC/HLA molecules and induce lysis of tumor cells (page 25 paragraph 104). However, the specification does teach which fragment or derived peptides claimed in the instant claims can be used to stimulate immune response and binds to one or more MHC molecules presented on the

surface of cells and elicit a cytolytic response. It is not clear if (CTLs) could be generated using any peptide fragment of SEQ ID:32 other than the peptides LLSHGAVIEV, SLSKILDTV, and SLDQKLFQL.

One cannot extrapolate the teaching of the specification to the claimed invention of claims 58-60 because there is no guidance on or exemplification of any correlation between any peptide derived from proteins encoded by nucleotides comprising SEQ ID NO:32, wherein capable of specifically activating cytotoxic T lymphocytes (CTLs) with claimed specifity/activity. The specification does not disclose common structural attributes that stimulate an immune response and binds to one or more MHC molecules presented on the surface of cells. There is insufficient guidance regarding the parameters and sequence of peptides which correlate with the ability to stimulate T cell with any MHC molecule and generate CTLs with claimed specifity/activity. There is insufficient guidance regarding selection of peptides that meet the instant criteria of stimulating T lymphocytes with specific activity. Thus, there is insufficient guidance regarding the parameters and sequences of peptides which correlate with the ability to be recognized by the specific CTL clone.

Roitt et al (Immunology, Fourth Edition, 1996, Mosby, page 7.9-7.11) teach that T cells recognizes cell-bound antigen in association with MHC molecules. MHC class I and class II act as guidance systems for T cells. This is known as MHC restriction. Only a minority of peptide fragments from a protein antigen is able to bind particular MHC molecules. Different MHC molecules bind different sets of peptides. Roitt et al specifically teach Fig. 7.22 and Fig. 7.23, and also page 7.10, right column that the

peptides sizes 12-15 are optimal for MHC molecule class I and certain amino acids at certain positions are critical for binding to MHC class I.

US Pat. 5,840,839 (Nov. 24, 1998) teach at column 19 that finding a peptide that binds to a MHC molecules and stimulates immune response is not a trivial matter. The '839 patent at column 19, lines 53 to 67 teaches that structure a T cell epitope that stimulates immune response in context of MHC molecules is unpredictable in the current state of art. The '839 patent at columns 19-20, and Table 1 teaches that the various candidate T cell epitopes selected based on theoretical binding motif of one class of MHC molecule, i.e. HLA-A31 do not work when they are experimentally tested as shown in Table 1. This suggests that theoretically selected T cell binding motifs have to be tested experimentally in order to determine whether they are actually T cell epitopes or not.

The specification provides insufficient guidance with regard to theses issues and provides limited working examples of any peptide that would work with any MHC molecule. Considering the state of art, the broad scope of claims in respect to the nature of peptide and also to the nature of MHC molecules, it is concluded that undue experimentation is required to practice the claimed invention. It is noted that law requires that the disclosure of an application shall inform those skilled in the art how to make the alleged discovery, not how to screen it for themselves.

8. Claims 13, 58-60, 85, and 86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 13, 58-60, 85, and 86 are drawn to genus of polypeptides comprising a fragment of SEQ ID NO: 32.

The applicable standard for the written description requirement can be found: MPEP 2163; University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407; PTO Written Description Guidelines; Enzo Biochem Inc. v. Gen-Prove Inc., 63 USPQ2d 1609; Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111; and University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC 2004).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial sequence. There is not even identification of any particular function associated with the claimed genus of polypeptides. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

The present claims 13, 58-60, 85, and 86 encompass full-length proteins encoded by differently spliced isoforms or homololgs that are not further described.

There is substantial variability among the species of polypeptides encompassed within the scope of the claims because the claims are construed with the transitional phrase "comprising" that only a partial sequence in the body of the claims. A description of a genus of full-length proteins may be achieved by means of a recitation of a representative number of proteins encoded by the corresponding the ORFs, defined by nucleotide sequences, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

Double Patenting

9. Claim 114 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 92. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Both claims are drawn to only one species, i.e. SEQ ID NO: 32.

Summary

10. No claims allowed.

The prior art does not disclose an isolated tumor antigen comprising the amino acid sequence of SEQ ID NO:32 encoded by the nucleic acid of SEQ ID NO:31.

Houghton et al (U.S. Patent No: 6,958,361, issued Oct 25, 2005, filed February 13, 2002) disclose a tumor antigen that has a 96% sequence identity to the amino acid sequence of SEQ ID NO:32 including a local similarity of 99.8% (see sequence search).

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from 8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Halvorson, PhD
Patent Examiner
571-272-6539

MISOOK YU
PRIMARY EXAMINER

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RESULT 2
US-10-076-622-565
; Sequence 565, Application US/10076622
; Patent No. 6958361
; GENERAL INFORMATION:
;  APPLICANT: Houghton, Raymond L.
;  APPLICANT:  Sleath, Paul R.
;  APPLICANT:  Persing, David H.
;  TITLE OF INVENTION: COMPOSITIONS AND METHODS FOR THE THERAPY
;  TITLE OF INVENTION:  AND DIAGNOSIS OF BREAST CANCER
;  FILE REFERENCE: 210121.470C11
;  CURRENT APPLICATION NUMBER: US/10/076,622
;  CURRENT FILING DATE:  2002-02-13
;  NUMBER OF SEQ ID NOS: 627
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 565
;   LENGTH: 1341
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-10-076-622-565

  Query Match             95.9%;  Score 6898;  DB 2;  Length 1341;
  Best Local Similarity   99.8%;  Pred. No. 0;
  Matches 1338;  Conservative    1;  Mismatches    2;  Indels    0;  Gaps    0;

Qy         57 MTKRKKTINLNIQDAQKRTALHWACVNGHEEVVTFLVDRKCQLDVLDGEHRTPLMKALQC 116
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Qy        117 HQEACANILIDSGADINLVDVYGNTALHYAVYSEILSVVAKLLSHGAVIEVHNKASLTPL 176
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Db         61 HQEACANILIDSGADINLVDVYGNMALHYAVYSEILSVVAKLLSHGAVIEVHNKASLTPL 120

Qy        177 LLSITKRSEQIVEFLLIKNANANAVNKYKCTALMLAVCHGSSEIVGMLLQQNVDVFAADI 236
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Qy        297 SLVEKTPDEAAPLVERTPDTAESLVEKTPDEAASLVEGTSDKIQCLEKATSGKFEQSAEE 356
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Qy        357 TPREITSPAKETSEKFTWPAKGRPRKIAWEKKEDTPREIMSPAKETSEKFTWAAKGRPRK 416
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Db        301 TPREITSPAKETSEKFTWPAKGRPRKIAWEKKEDTPREIMSPAKETSEKFTWAAKGRPRK 360

Qy        417 IAWEKKETPVKTGCVARVTSNKTKVLEKGRSKMIACPTKESSTKASANDQRFPSESKQEE 476
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Qy        477 DEEYSCDSRSLFESSAKIQVCIPESIYQKVMEINREVEEPPKKPSAFKPAIEMQNSVPNK 536
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Qy        537 AFELKNEQTLRADPMFPPESKQKDYEENSWDSESLCETVSQKDVCLPKATHQKEIDKING 596
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Qy       837 EESPDNDGFLKAPCRMKVSIPTKALELMDMQTFKAEPPEKPSAFEPAIEMQKSVPNKALE 896
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Qy       897 LKNEQTLRADQMFPSESKQKKVEENSWDSESLRETVSQKDVCVPKATHQKEMDKISGKLE 956
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Qy       957 DSTSLSKILDTVHSCERARELQKDHCEQRTGKMEQMKKKFCVLKKKLSEAKEIKSQLENQ 1016
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Qy      1017 KVKWEQELCSVRLTLNQEEEKRRNADILNEKIREELGRIEEQHRKELEVKQQLEQALRIQ 1076
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Qy      1077 DIELKSVESNLNQVSHTHENENYLLHENCMLKKEIAMLKLEIATLKHQYQEKENKYFEDI 1136
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Db      1021 DIELKSVESNLNQVSHTHENENYLLHENCMLKKEIAMLKLEIATLKHQYQEKENKYFEDI 1080

Qy      1137 KILKEKNAELQMTLKLKEESLTKRASQYSGQLKVLIAENTMLTSKLKEKQDKEILEAEIE 1196
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Qy      1197 SHHPRLASAVQDHDQIVTSRKSQEPAFHIAGDACLQRKMNVDVSSTIYNNEVLHQPLSEA 1256
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Qy      1257 QRKSKSLKINLNYAGDALRENTLVSEHAQRDQRETQCQMKEAEHMYQNEQDNVNKHTEQQ 1316
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Qy      1317 ESLDQKLFQLQSKNMWLQQQLVHAHKKADNKSKITIDIHFLERKMQHHLLKEKNEEIFNY 1376
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Qy      1377 NNHLKNRIYQYEKEKAETENS 1397
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Db      1321 NNHLKNRIYQYEKEKAETENS 1341
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